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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/762,959	01/21/2004	David A. Griffith	PC25408A	7298

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PATENT DEPARTMENT, MS8260-1611
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EXAMINER	
MCKENZIE, THOMAS C	

ART UNIT	PAPER NUMBER
1624	

DATE MAILED: 04/19/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/762,959	GRIFFITH, DAVID A.	
	Examiner	Art Unit	
	Thomas McKenzie, Ph.D.	1624	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *02 January 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-127* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-127* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *1/04,8/04,8/04&12/04*
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

1. This action is in response to an application filed on 1/2/04. There are one hundred twenty-seven claims pending and one hundred twenty-seven under consideration. Claims 1-94 and 123-127 are compound claims. Claims 95-98 are composition claims. Claims 99-122 are method of using claims. This is the first action on the merits. The application concerns some pyrazolo[1,5-a]pyrimidine compounds, compositions, and uses thereof.

Title

2. The title of the invention is not descriptive. A new title is required that is clearly indicative of the invention to which the claims are directed. The following title is suggested: addition of the word " Pyrazolo[1,5-a]pyrimidine" to the beginning of the title.

Claim Rejections - 35 USC § 112

3. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 99-103, 106-109, 111-115, and 118-122 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The specification does not set forth any steps involved in determining how to identify "a disease, condition or disorder which is modulated by a cannabinoid antagonist".

It is unclear what diseases and treatments applicant is intending to encompass. Determining whether a given disease responds or does not respond to such a receptor antagonist and thus, covered by the claim language, will require extensive and potentially inconclusive clinical research. With out such clinical research to identify the patients and diseases Applicants intend to treat, the physician skilled in the clinical arts cannot determine the metes and bounds of the claim. Hence, the claims are indefinite. The passage in the specification spanning line 22, page 27 to line 13, page 28 gives an impressively long list of such diseases. However, that passage uses the open term "includes". What other diseases, in addition to those listed, are being claimed? The Examiner suggests listing the specific diseases, which Applicant intends to treat being mindful of the enablement rejection made below.

4. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-127 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for making salts of the claimed compounds, does not reasonably provide enablement for making solvates, prodrugs, and hydrates of the claimed compounds. The specification does not enable any person

skilled in the art of synthetic organic chemistry to make the invention commensurate in scope with these claims. "The [eight] factors to be considered [in making an enablement rejection] have been summarized as a) the quantity of experimentation necessary, b) the amount of direction or guidance presented, c) the presence or absence of working examples, d) the nature of the invention, e) the state of the prior art, f) the relative skill of those in that art, g) the predictability or unpredictability of the art, h) and the breadth of the claims", *In re Rainer*, 146 USPQ 218 (1965); *In re Colianni*, 195 USPQ 150, *Ex parte Formal*, 230 USPQ 546. In the present case the important factors leading to a conclusion of undue experimentation are the absence of any working example of a formed solvate or prodrug, the limited guidance provided by the specification, the lack of predictability in the art, and the broad scope of the claims.

b) The direction concerning the solvates is found in the passage spanning line 25, page 35 to line 2, page 36. No specific solvates are mentioned and no direction for making any solvate is disclosed. The direction concerning the prodrugs is found in the passage spanning line 27, page 49 to line 10, page 51. Prodrug derivatives for three specific functional groups are taught.

c) There is no working example of any prodrug, hydrate, or solvate formed. The claims are drawn to prodrugs and solvates, yet the numerous examples

presented all failed to produce a solvate. These cannot be simply willed into existence. As was stated in *Morton International Inc. v. Cardinal Chemical Co.*, 28 USPQ2d 1190 "The specification purports to teach, with over fifty examples, the preparation of the claimed compounds with the required connectivity. However ... there is no evidence that such compounds exist... the examples of the '881 patent do not produce the postulated compounds... there is ... no evidence that such compounds even exist." The same circumstance appears to be true here. There is no evidence that solvates of these compounds actually exist; if they did, they would have formed. Hence, applicants must show that solvates can be made, or limit the claims accordingly.

e) The state of the solvate art is that is not predictable whether solvates will form or what their composition will be. In the language of the physical chemist, a solvate of organic molecule is an interstitial solid solution. This phrase is defined in the second paragraph on page 358 of West (Solid State Chemistry). The solvent molecule is a species introduced into the crystal and no part of the organic host molecule is left out or replaced. In the first paragraph on page 365, West (Solid State Chemistry) says, "it is not usually possible to predict whether solid solutions will form, or if they do form what is their compositional extent". Thus, in the absence of experimentation one cannot predict if a particular solvent will solvate

any particular crystal. One cannot predict the stoichiometery of the formed solvate, i.e. if one, two, or a half a molecule of solvent added per molecule of host. In the same paragraph on page 365 West (Solid State Chemistry) explains that it is possible to make meta-stable non-equilibrium solvates, further clouding what Applicants mean by the word solvate. Compared with polymorphs, there is an additional degree of freedom to solvates, which means a different solvent or even the moisture of the air that might change the stabile region of the solvate.

Wolff (Medicinal Chemistry) summarizes the state of the prodrug art. The table on the left side of page 976 outlines the research program to be undertaken to find a prodrug. The second paragraph in section 10 and the paragraph spanning pages 976-977 indicate the low expectation of success. In that paragraph the difficulties of extrapolating between species are further developed. Since, the prodrug concept is a pharmacokinetic issue, the lack of any standard pharmacokinetic protocol discussed in the last sentence of this paragraph is particularly relevant. Banker (Modern Pharmaceutics) in the first sentence, third paragraph on page 596 states that "extensive development must be undertaken" to find a prodrug.

h) The breadth of the claims includes all of the millions of compounds of formula (I) as well as the presently unknown list of solvents embraced by the term "solvate". Thus, the scope is broad.

MPEP 2164.01(a) states, "A conclusion of lack of enablement means that, based on the evidence regarding each of the above factors, the specification, at the time the application was filed, would not have taught one skilled in the art how to make and/or use the full scope of the claimed invention without undue experimentation. *In re Wright*, 999 F.2d 1557,1562, 27 USPQ2d 1510, 1513 (Fed. Cir. 1993)." That conclusion is clearly justified here. Thus, undue experimentation will be required to practice Applicants' invention.

The Examiner suggests claiming the specific prodrug derivatives listed in the passage spanning line 27, page 49 to line 10, page 51 and omitting claims to solvates.

5. Claims 1-8, 11-16, 20-24, 27-32, 36-40, 43-45, 48-82, 84-86, 88-93, 95-127 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for using the compounds of formula (I) with $R^0 = R^1$ = halogen substituted phenyl, does not reasonably provide enablement for using the compounds of formula (I) with $R^0 = R^1$ = substituted aryl generally or heteroaryl. The specification is not adequately enabled for the scope of fused rings that have

functional groups attached to radicals R^0 and R^1 and differing heteroaryl rings. Compounds made and tested represent the scope of claim 9, 17-19, 25, 26, 33-35, 41, 42, 46, 47, 83, 87, and 94, not claim 1. The specification does not enable any skilled pharmacologist or physician to use the invention commensurate in scope with these claims. The factors to be considered in making an enablement rejection have been summarized above.

a) Determining if any particular claimed compounds with $R^0 = R^1 =$ substituted aryl generally or heteroaryl would be active would require synthesis of the substrate and subjecting it to testing with Applicants' *in vitro* CB-1 receptor binding assay. Considering the large number of compounds to be made this is a large quantity of experimentation. b) The direction concerning the claimed $R^0 = R^1 =$ substituted aryl generally or heteroaryl compounds is found in lines 7-20, page 4, which merely states Applicants intent to make and use such compounds. c) In the instant case none of the working examples contains any fluoro, trifluoromethyl, alkyl, or alkoxy radical attached to a phenyl $R^0 = R^1 =$ group. None of these working examples contain a basic or acidic group attached to a R^0 or R^1 substituent. . None of these R^0 or R^1 substituents contain electron deficient hetero aromatic rings.

d) The nature of the invention is antagonism of the CB-1 receptor and treatment of human diseases with Applicants' compounds. This involves physiological activity. The nature of the invention requires an understanding of the CB-1 receptor, the binding activity of small ligands to that receptor, and the ability of those compounds to inhibit the functioning of the CB-1 receptor. In view of the unpredictability of receptor binding activity and claimed divergent substituents with varied polarity, size, and polarisability, the skilled physician would indeed question the inclusion of such diverse rings, commensurate in scope with these claims. Also see the MPEP § 2164.03 for enablement requirements in the structure sensitive arts of pharmacology and medicinal chemistry.

e) The state of the art is detailed knowledge of the CB-1 receptor is lacking. No X-ray structure of the receptor is known and the structural requirements of ligands to this receptor are poorly understood. The six-membered benzene ring radicals of the R^0 and R^1 substituent of Applicants' working example compounds is non-basic. The pyridine ring, pyridazine ring, and the pyrazine ring of the rejected compounds are strongly basic, basic, and weakly basic respectively. The pyridine ring and the pyrazine ring of the rejected compounds are hydrogen bond acceptors. The benzene ring of Applicants working examples is not. The pyridine ring and the pyrazine ring of the rejected compounds are π-electron deficient. The benzene

ring of Applicants working examples is not. There is no reasonable basis for the assumption that the myriad of compounds embraced the present formula (I) will all share the same biological properties. For example, the rings include pyrimidine and triazine radicals with two or three extra basic sites. The rings include thiophenes with additional polarizable sulfur atoms. The rejected rings include sterically large quinoline and purine rings. The diverse claimed fused heteroaryl rings are chemically non-equivalent and there is no basis in the prior art for assuming in the non-predictable art of CB-1 receptor pharmacology that structurally dissimilar compounds will have such activity, *In re Surrey* 151 USPQ 724. Compounds made and tested represent the scope of claims 9, 17-19, 25, 26, 33-35, 41, 42, 46, 47, 83, 87, and 94 not claim 1.

f) The artisan using Applicants invention to treat diseases with the claimed compounds would be a physician with a MD degree and several years of experience. He would be unaware of how to predict *a priori* how a changing a heterocyclic ring would affect biological activity. In view of the divergent rings with varied basicity, steric hindrance, and polarisability, the skilled physician would indeed question the inclusion of such fused rings, commensurate in scope with these claims. g) Physiological activity, is well-known to be unpredictable, *In re Fisher*, 427 F.2d 833, 839, 166 USPQ 18, 24 (CCPA 1970) (contrasting

mechanical and electrical elements with chemical reactions and physiological activity). See also *In re Wright*, 999 F.2d 1557, 1562, 27 USPQ2d 1510, 1513 (Fed. Cir. 1993); *In re Vaeck*, 947 F.2d 488, 496, 20 USPQ2d 1438, 1445 (Fed. Cir. 1991). h) The breadth of the claims includes all of millions of compounds of formula (I). Thus, the scope is very broad. The present claims embrace various heterocyclic radicals, which are not art-recognized as equivalent. The specific compounds made are not adequately representative of the compounds embraced by the extensive Markush groups instantly claimed.

MPEP 2164.01(a) states, "A conclusion of lack of enablement means that, based on the evidence regarding each of the above factors, the specification, at the time the application was filed, would not have taught one skilled in the art how to make and/or use the full scope of the claimed invention without undue experimentation. *In re Wright*, 999 F.2d 1557,1562, 27 USPQ2d 1510, 1513 (Fed. Cir. 1993)." That conclusion is clearly justified here. Thus, undue experimentation will be required to practice Applicants' invention.

6. Claims 99-122 rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for blocking the acute psychological and physiological effects of smoked marijuana and for treating obesity, does not reasonably provide enablement for treating Parkinson's Disease, dementia, or any

of the other specifically listed diseases whose treatment is claimed. The specification does not enable any physician skilled in the art of medicine, to make the invention commensurate in scope with these claims. The how to make requirement of the enablement statute, when applied to process claims, refers to operability and how to make the claimed process work. The eight factors to be considered in making an enablement rejection have been summarized above. The three main issues are the lack of any correlation between clinical efficacy for Parkinson's Disease, dementia, or any of the other specifically listed diseases whose treatment is claimed treatment and Applicants' three *in vitro* assays, the state of the prior art, and the breadth of the claims.

There is an *in vitro* assay, drawn to inhibition of binding to the CB-1 receptor, described in the passage spanning line 10, page 119 to line 26, page 120 with no specific data. Applicants state that their 48 final working example compounds, "provided a range of binding activities from 0.2-155nM". Both human and rat receptor assays are described and it is unclear which of these two receptor types were used. Applicants do not state and it is not recognized in the therapeutic arts this assay is correlated to clinical efficacy for treating Parkinson's Disease, dementia, or any of the other specifically listed diseases whose treatment is claimed.

There is an *in vitro* assay, drawn to inhibition of $GTP_{\gamma}[^{35}S]$ binding to the CB-1 receptor, described in the passage spanning line 20, page 121 to line 7, page 122 with no specific data. There is a CB-2 *in vitro* receptor binding assay described in the passage spanning line 27, page 130 to line 19, page 121, again with no specific data. There are seven *in vivo* assays described on pages 123-129 but there are merely prophetic.

The state of the clinical arts with CB-1 receptor antagonists is provided by Huestis (Arch Gen Psychiatry.) who reports that the antagonist SR141716 blocked acute psychological and physiological effects of smoked marijuana. Giuffrida (J. Pharmacol. Exp. Ther.) reports in the first paragraph, page 13 "the CB-1 receptor antagonist SR141716A exacerbates pain when administered alone". Pertwee (Forsch Komplementarmed.) reports "CB1 receptor antagonists may also have clinical applications, e. g. as appetite suppressants and in the management of schizophrenia or disorders of cognition and memory". This implies that such clinical uses were not art-recognized in 1999. The state of the clinical arts in CB1 antagonist pharmacology is provided by Barth (Curr Med Chem.), who writes "the recent development of cannabinoid antagonists belonging to other chemical series illustrates the interest of these compounds which are now considered as interesting therapeutic targets". Thus, therapeutic use of such antagonists was still in the

experimental stage in 1999 and was speculative in nature. Substantiation of use and scope is required when the use is "speculative", "sufficiently unusual", or not provided in the specification, *Ex parte Jovanovics,* 211 USPQ 907, *In re Langer,* 183 USPQ 288, *Hoffman v. Klaus*, 9 USPQ2d 1657, and *Ex parte Powers*, 200 USPQ 925 concerning the type of testing needed to support *in vivo* use claims. Also see the MPEP § 2164.03 for enablement requirements in the structure sensitive arts of pharmacology and medicinal chemistry.

Brotchie (Curr Opin Pharmacol.) reports in his abstract that, "[r]ecent studies in animal models and in the clinic suggest that CB(1) receptor antagonists could prove useful in the treatment of Parkinsonian symptoms and levodopa-induced dyskinesia". Ruiu (Pharmacol Exp Ther.) writes in the fianl paragraph, firt column, on page 369, "[a]dditional *in vivo* experiments should provide further evidence for the clinical potential of this powerful CB_1 antagonist. It should be determined whether NESS 0327 would show better efficacy as a CB_1 antagonist in animal models of excessive food intake, psychosis, and cognitive impairment, three areas of possible interest for a novel CB_1-selective antagonist." "[C]ould" or "possible" are not the standards for enablement of disease treatment claims, which requires in an unpredictable art, such as disease therapy a well-established correlation between the *in vitro* assay and clinical efficacy.

Tzavara (Br J Pharmacol.) reports in the first complete pargarph, second column, page 544, that the CB1 antagonist, "SR141716A also suppresses both palatable and non-palatable food intake under operant and non-operant experimental schedules in animals (reviewed in Chaperon & Thiebot, 1999.) and reduces body weight of obese patients (communicated by G. Le Fur, 2001, International Cannabinoid Research Society Meeting, El Escurial, Spain)." Thus, prior to Applicants' effective filing date in 2003 treatment of obesity was an art-recognized clinical use of such antagonists.

The state of the art in Parkinson's treatment is provided by Anonymous, (Drug Therap. Bull.), who lists l-DOPA, COMT inhibitors, MOA-B inhibitors, and dopamine agonists as newly developed treatments. There is no mention of the CB-1 receptor antagonists of the present application. Burke (Post Graduate medicine) in his review "Update on Alzheimer's Disease" on pages 90-96, final paragraph lists cholinesterase inhibitors, vitamin E, estrogen, and nonsteroidal anti-inflammatory drugs as possible treatments of the symptoms of Alzheimer's disease. Alzheimer's disease is a form of dementia, currently claimed. There is no mention of either the pyrazolo[1,5-a]pyrimidine compounds of the present Application or of CB-1 antagonists generally. Shoulson (Science) in Table 1, page 1073 says regarding Alzheimer's disease treatment "symptomatic therapy- cholinergic

agents". Thus, the only art-recognized agents for treating Alzheimer's disease are cholinergic agents.

The scope of the claims involves all of the millions of compounds of claim 1 as well as the unknown scope of diseases embraced by the term "a disease, condition or disorder which is modulated by a cannabinoid antagonist". Thus, the scope of claims is very broad.

MPEP §2164.01(a) states, "A conclusion of lack of enablement means that, based on the evidence regarding each of the above factors, the specification, at the time the application was filed, would not have taught one skilled in the art how to make and/or use the full scope of the claimed invention without undue experimentation. *In re Wright*, 999 F.2d 1557,1562, 27 USPQ2d 1510, 1513 (Fed. Cir. 1993)." That conclusion is clearly justified here and undue experimentation will be required to practice Applicants' invention.

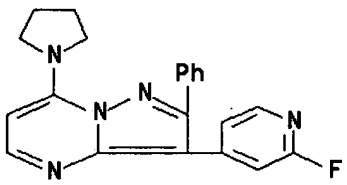
Claim Rejections - 35 USC § 102

7. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this

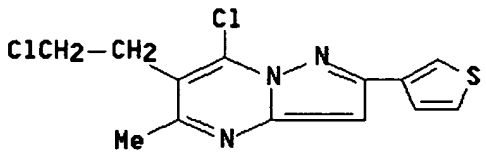
subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

Claims 1, 2, 95, and 96 are rejected under 35 U.S.C. 102(e) as being anticipated by Gudmundsson (US 2005/0203106 A1). The compound shown below fits formula (I) with R^0 = phenyl, R^1 = 2-fluoro-4-pyridinyl, $R^2 = R^3 = R^{4f} = R^{4f'} = R^{4b} = R^{4b'} = R^{4d} = R^{4d'} = R^{4e} = R^{4e'}$ = hydrogen, R^4 = Formula (IA), X = a bond, Y = -$C(R^{4d})(R^{4d'})$-, and Z = -$C(R^{4e})(R^{4e'})$-. It has Registry Number 625095-77-4 and is found in paragraph [0217], page 17 of the reference. It is Example 1 and synthesis is taught in paragraphs [0225] and [0226] on page 18. A second anticipatory compound is Example 2 in paragraph [0227]. Compositions of the taught compounds are taught in claims 19 and 20 of the reference. Claim 21 of the reference teaches a composition containing the additional pharmaceutical agents acyclovir and valqciclovir. Thus the present claims 95 and 96 are also anticipated.

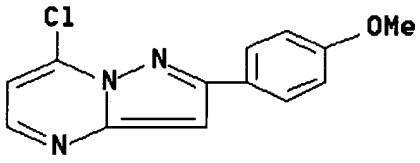


8. Claim 123 is rejected under 35 U.S.C. 102(b) as being anticipated by Tsujitani ('442). The compound shown below fits formula (Id) with R^0 = 3-thienyl, R^2 = methyl, R^3 = 2-chloroethyl, and X = chlorine. It has Registry Number

129909-72-4 and is found in lines 46-54, column 7 of the reference. It is Example VI(v) and physical properties are taught in lines 55-58, column 7. Synthesis is taught in lines 29-30, column 7.



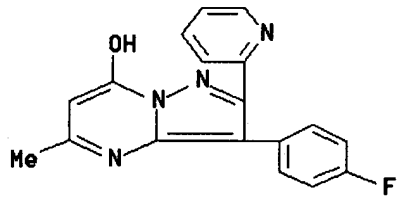
9. Claim 123 is rejected under 35 U.S.C. 102(e) as being anticipated by Gudmundsson (US 2005/0203106 A1). The compound shown below fits formula (Id) with R^0 = 4-methoxyphenyl, R^2 = R^3 = hydrogen, and X = chlorine. It has Registry Number 625095-88-7 and is found in lines 1-2, paragraph [0237], page 17 of the reference.



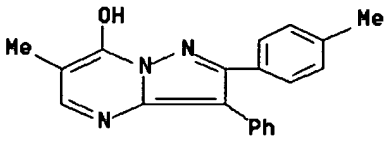
10. Claim 124 is rejected under 35 U.S.C. 102(e) as being anticipated by Gudmundsson (US 2005/0203106 A1). The product of the reaction between the compound pictured above and N-iodosuccimide fits formula (Ie) with R^0 = 4-methoxyphenyl, R^2 = R^3 = hydrogen, and X = chlorine. The 3-iodo compound was

not isolated but reacted *in situ* with cyclopentylamine. However, there can be no doubt the 3-iodo-7-chloro compound, claimed by Applicants, was made by the reference.

11. Claim 126 is rejected under 35 U.S.C. 102(b) as being anticipated by Inoe (JP 05/125079 A1). The compound shown below fits formula (4d) with R^0 = 2-pyridyl, R^1 = 4-fluorophenyl, R^2 = methyl, and R^3 = hydrogen. It has Registry Number 150130-99-7 and is found in column 17 of the reference. It is Example 21.



12. Claim 126 is rejected under 35 U.S.C. 102(b) as being anticipated by Inoue ('951). The compound shown below fits formula (4d) with R^0 = 2-methylphenyl, R^1 = phenyl, R^2 = hydrogen, and R^3 = methyl. It has Registry Number 189018-07-3 and is found in column 21 of the reference. It is Example 23. See also compound 31 in column 23.

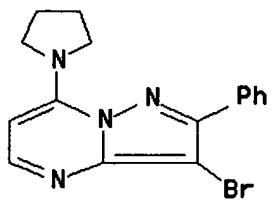


Claim Rejections - 35 USC § 103

13. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claim 125 is rejected under 35 U.S.C. 103(a) as being unpatentable over Gudmundsson (US 2005/0203106 A1). The reference teaches the compound with registry number 625095-84-3 shown below. The Applicant claims the compound of (If) with R^0 = phenyl, $R^2 = R^3 = R^{4f} = R^{4f'} = R^{4b} = R^{4b'} = R^{4d} = R^{4d'} = R^{4e} = R^{4e'}$ = hydrogen, R^4 = Formula (IA), X = a bond, Y = $-C(R^{4d})(R^{4d'})-$, Z = $-C(R^{4e})(R^{4e'})-$, and iodine in position 3 of the pyrazolo[1,5-a]pyrimidine ring. The reference teaches a compound with bromine in position 3 of the pyrazolo[1,5-a]pyrimidine ring. The compound shown in the reference in paragraphs [0223] and [0224], page



18. The difference between the claimed and taught compounds is the replacement of bromine in the taught compound with iodine in the claimed compound. The equivalence of iodine and bromine is taught in the reference in the formula VII in paragraph [0167], page 12. The definition of variable X in formula VII is provided in paragraph [0159], page 11 of the reference. The compound taught in the reference is an intermediate but it is used for the same purpose as Applicants claimed compound (If), namely as a partner in a Suzuki aryl coupling reaction to make a biologically active compound. Applicants' claimed iodine leaving group often gives higher yields under milder conditions that the bromine leaving group of the taught compound in the Suzuki process. That would provide the motivation to the skilled organic process chemist to make the change in halogen atoms.

Conclusion

14. Information regarding the status of an application should be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at (866) 217-9197 (toll-free). Please

direct general inquiries to the receptionist whose telephone number is (703) 308-1235.

15. Please direct any inquiry concerning this communication or earlier communications from the Examiner to Thomas C McKenzie, Ph. D. whose telephone number is (571) 272-0670. The FAX number for amendments is (571) 273-8300. The PTO presently encourages all applicants to communicate by FAX. The Examiner is available from 9:00am to 5:30pm, Monday through Friday. If attempts to reach the Examiner by telephone are unsuccessful, please contact James O. Wilson, SPE of Art Unit 1624, at (571)-272-0661.

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TCMcK/me